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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/424,519	03/03/2000	JAMES B. MITCHELL	175931	8084

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 05/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/424,519	MITCHELL ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2004 and 22 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-21,28 and 30-49* is/are pending in the application.

4a) Of the above claim(s) *4-21 and 31-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,28, 30 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 March 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicants' filing of this application as RCE under 37 CFR 1.114. Claims 1, 28, 30 and 49 are currently pending for the prosecution on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 28, 30 and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating ataxia telangiectasia or Li Fraumeni syndrome with tempol, does not reasonably provide enablement for "a method for the therapeutic treatment cancer...due to a genetic defect in p53 gene", " a method for prophylactic or therapeutic treatment of cancer in an animal...ataxia telangiectasia or Li Fraumeni syndrome" or " a method for the prophylactic treatment of cancer in an animal" with "nitroxide or prodrug thereof...a compound of Formula I or II". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d

1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

Claim 1 is directed to a method for the therapeutic treatment of cancer due to a genetic defect in the p53 gene; claim 28 is directed to a method for the prophylactic or therapeutic treatment of cancer due to ataxia telangiectasia or Li Fraumeni syndrome; and claims 30 and 49 are directed to a method for the prophylactic treatment of cancer.

(2) The state of the prior art

There are no known compounds of similar structure which have been demonstrated to treat or prevent all types of cancers or cancers due to a genetic defect in the p53 gene. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "silver bullet" is contrary to our present understanding of oncology. Cecil Textbook of Medicine states that "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different method of growth and harm the body. Also see In re Buting, 163 USPQ 689 (CCPA 1969), wherein 'evidence involving a single compound and two types of

cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers'. Thus, it is beyond the skill of oncologists today to get an agent to be effective against all cancers or cancers due to a genetic defect in the p53 gene.

With respect to the instantly claimed "prophylactic treatment of cancer" or "prophylactic treatment of ataxia telangiectasia or Li Fraumeni syndrome", the state of art does not recognize the administration of any compounds or compositions to prevent or completely eliminate (cure) the cancers or ataxia telangiectasia or Li Fraumeni syndrome as required in the instant claims (see "NINDS Ataxia Telangiectasia Information Page", The National Institute of Neurological Disorders and Stroke, NIH, 2003; "Genetic Testing on Embryos Hits New Milestone", Matloff, E., Reuters News, 2001).

(3) The relative skill of those in the art

The relative skill of those in the art of pharmaceuticals is high.

(4) The predictability or unpredictability of the art

The specification does not provide any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(5) The breadth of the claims

The instant claims embrace the prophylactic or therapeutic treatment of all cancers due to a genetic defect in p53 gene (claims 1 and 49) and the prophylactic treatment of all cancers

(claim 30). The instant claims cover "cancers" that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

The breadth of the claims is further exacerbated by the instantly claimed plethora of compounds that are described as being a nitroxide or prodrug thereof represented by compound of Formula I or II.

(6) The amount of direction or guidance presented

The specification discloses the results of study involving Tempol or sugar-water treated p53 knock-out mice (KO1), wherein the study shows that both Tempol-treated mice and sugar-water-treated mice group ultimately develop cancers, but the percent survival is increased in Tempol-treated group (page 16, lines 4-6). Declaration, filed 9/22/03, shows that Tempol is useful in prolonging the lifespan of p53 deficient mice.

Although the specification and the Declaration provide enabling disclosure for delaying onset or progression of the specific cancers due to p53 gene mutations (i.e., ataxia telangietasia or Li Fraumeni syndrome) with the administration of Tempol, none of the specification or the Declaration provides enabling disclosure for the claimed prophylactic or therapeutic treatment of all cancers or the entire scope of cancers due to a genetic defect in p53 gene. Furthermore, there is insufficient evidences for the claimed prophylactic use of Tempol in preventing or eliminating (completely) of said cancers (i.e., ataxia telangiectasia or Li Fraumeni syndrome), and for enablement in making/using vast number of possible compounds and the genus of formula or II for the treatment or prevention of said cancers that may or may not be related to p53 gene. The specification provides no guidance, in the way of enablement for the full scope of all compounds of formula I or II that are potentially suitable for the invention work similarly as to Tempol. The

skill artisan would have not known that which compounds of the claimed compounds of formula I or II are capable of accomplishing the desired result of the claimed invention without undue amount of experimentation.

(7) The presence or absence of working examples

As stated above, the specification and the Declaration only provide the usefulness of Tempol in prolonging the lifespan of p53 deficient mice or p53 knock-out mice (KO1). Both specification and the Declaration fail to provide adequate representation regarding the conclusion of the efficacy of Tempol in treating or preventing all cancers or any cancers due to a genetic defect in p53 gene from applicant's showing of the efficacy of Tempol in increasing the percent survival in p53 "knock-out" or p53 deficient mice model study, other than the therapeutic treatment of ataxia telangiectasia or Li Fraumeni syndrome.

(8) The quantity of experimentation necessary

Since the efficacy of Tempol in preventing or treating various types of cancers mentioned above or all cancers due to p53 gene mutation cannot be predicted from a priori but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to use the invention commensurate in scope with the claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 28, 30 and 49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22 of U.S. Patent No. US 5,462,946 or claim 2 of US 6,605,619. Although the conflicting claims are not identical, they are not patentably distinct from each other because the prior methods of administering 4-hydroxy-2,2,6,6,-tetramethylpiperidine-1-oxyl (Tempol) to mammals or organisms (at risk for developing cancer) must inherently possess a prophylactic utility of the claimed invention.

Since the referenced effective dosage amounts (See page 15, lines 56-66 of US'619 and claim 22 of US'946) overlap with the claimed prophylactic dosage amount "prevent cancer" (about 0.1 to about 100mg/kg/body weight, See page 11, lines 5-11 of the instant specification), the referenced methods make obvious the claimed invention.

Since the referenced mammals or organisms are also at risk for developing cancer as to the instant invention, the referenced methods make obvious the claimed invention.

Conclusion

4. No Claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (571) 273-0584. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614

Vickie Kim
PRIMARY EXAMINER
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